

### **REMARKS**

Claim 1 has been amended to recite, “[a] process for producing vitamin C from L-sorbose which comprises contacting L-sorbose with a purified L-sorbose dehydrogenase having the following physico-chemical properties: (a) Molecular weight:  $150,000 \pm 6,000$  Da or  $230,000 \pm 9,000$  Da (consisting of 2 or 3 homologous subunits, each subunit having a molecular weight of  $75,000 \pm 3,000$  Da)... (d) Optimum pH: 6.4 to 8.2... e) Inhibitors:  $\text{Co}^{2+}$ ,  $\text{Cu}^{2+}$ ,  $\text{Fe}^{2+}$ ,  $\text{Ni}^{2+}$ ,  $\text{Zn}^{2+}$ , monoiodoacetate and ethylenediamine tetraacetic acid...” The amendments were made to correct typographical errors. Support for these amendments are found in the specification at, for example, page 1, lines 16-28.

Claims 3 and 4 have been amended to recite “[t]he process according to claim 1, wherein the contacting of L-sorbose with a purified L-sorbose dehydrogenase is carried out...” The amendments were made for purposes of clarity and do not alter the scope of the claim. Support for these amendments are found in the original claims 3 and 4 and in the specification at, for example, page 4, lines 6-9. See *In re Gardner*, 177 USPQ 396, 397 (CCPA 1973) and MPEP §§ 608.01(o) and (l).

Claims 5-8 have been added. Support for claims 5-6 may be found in the specification at, for example, Example 3 (page 8). Support for claims 7-8 may be found in the specification at, for example, Example 2 (pages 7-8).

### **Obviousness Rejection**

Claims 1-4 were solely rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent Number 6,242,233 by Honma *et al.* (Paper No. 20071124 at 2).

Initially, we note that there is a factual error in the rejection. The first named inventor of the '233 patent is **Hoshino**, not "**Honma**" as the rejection states (and we note neither of the other two co-inventors are named Honma). Moreover, the rejection exclusively cites to "Honma". Thus, the rejection is, at best, ambiguous and should be withdrawn for this reason alone.

In an effort to further prosecution, in our Response, we assume the rejection is based on Hoshino *et al.*, U.S. Patent No. 6,242,233 ("Hoshino"). Accordingly, all of our comments herein are based on this assumption. If our assumption is incorrect, we request that the rejection be withdrawn as set forth above or reissued.

For the reasons set forth below, the rejection respectfully is traversed.

Hoshino discloses a new aldehyde dehydrogenase, which oxidizes L-sorbose to 2-keto-L-gulonic acid (2-KGA) in the presence of electron acceptors. (Hoshino, column 1, lines 35-41). Hoshino also discloses a process for producing 2-KGA from L-sorbose using the novel aldehyde dehydrogenase. (Hoshino, column 2, lines 59-63.)

In making the rejection, the Examiner asserted that Hoshino discloses:

a[n] L- sorbosone [sic] which is within the scope of the claimed product:

A new aldehyde dehydrogenase having the physico-chemical properties: molecular weight: 150,000.+-.6,000 or 230,000.+-.9,000 [sic]; substrate specificity: active on aldehyde compounds; cofactors: pyrroloquinoline quinone and heme c; optimum pH: 7.0-8.5; and inhibitors: ... (*Id.* at 3)

The Examiner also asserted that Hoshino discloses "a novel enzyme, namely aldehyde dehydrogenase (ADH), a process for producing ADH and a process for producing 2-keto-L-gulonic acid (2-KGA) from L-sorbosone utilizing said enzyme". (*Id.*, emphasis original). The Examiner also acknowledged that "2-KGA is an important intermediate for the production of vitamin C." (*Id.*, emphasis original). The Examiner then concluded that "[o]ne of ordinary skilled [sic] in the pertinent art would reasonably expect to prepare L-sorbosone utilizing the **ADL** which would be further processed to produce vitamin C based on the above reference." (*Id.*, emphasis added). The Examiner further concluded that "[i]f there are any differences with respect to various process conditions including reagents, concentrations, pH, reaction time, these differences would have been prima facie obvious to one of ordinary skilled [sic] in the pertinent art absent patentable differences." (*Id.*)

It is well settled the Examiner bears the burden to set forth a *prima facie* case of unpatentability. *In re Glaug*, 62 USPQ2d 1151, 1152 (Fed. Cir. 2002); *In re Oetiker*, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992); and *In re Piasecki*, 223 USPQ 785, 788 (Fed. Cir. 1984). If the PTO fails to meet its burden, then the applicant is entitled to a patent. *In re Glaug*, 62 USPQ2d at 1152.

We first note that the rejection fails to identify the differences between the presently claimed process and the cited document. But this is clear error. Indeed, the Examiner concedes that “[a]scertaining the differences between the prior art and the claims at issue” is required under *Graham*. (Paper No. 20071124 at 2). And, the Board has repeatedly counseled Examiners that they are “**required to specifically identify each difference** between **a claim**, on the one hand, and the disclosure of a reference or **a claim** of a reference that is relied upon, on the other. See *Ex parte Rozzi*, 63 USPQ2d 1196, 1201 (BPAI 2002) (“the Examiner has not cogently explained how Hill renders the subject matter of claim 1 obvious within the meaning of 35 USC § 103(a). A major difficulty with the rejection is that the PTO has failed to make a finding with respect to a difference, if any, between the subject matter of claim 1 and Hill.”). As explained in *Ex parte Braeken*, 54 USPQ2d 1110, 1112-13 (BPAI 1999) (unpublished), in making any art based rejection, the PTO must (1) identify all differences between each claim and the disclosure of a reference relied upon, and (2) explain why the subject matter of the claim, as a whole, would have been obvious notwithstanding the differences:

The Examiner acknowledges that there are differences between the subject matter of the claims and Christenson. Finding 5. But, the Examiner does not articulate with any particularity the precise nature of those differences. We decline to search the Christenson patent to ferret out those differences. ***Rather, findings with respect to the differences between claimed subject matter and the prior art are the responsibility of the Examiner in the first instance.*** [At 1112].

\* \* \*

***After all differences are identified, the Examiner should then explain why the subject matter of the claim, as a whole, would have been obvious notwithstanding the difference or differences.*** Until the differences are identified and the Examiner explains why the claimed subject matter, as a whole, would have been obvious, the appeal is not ripe for decision. [At 1113].

Because the Examiner failed to identify any difference between the recited claims and the cited art, the rejection is insufficient as a matter of law and must be withdrawn.

In addition, as the Examiner acknowledges, “an explanation for the reasoning that leads to a legal conclusion of obviousness for rejecting claims on that ground” is still required to establish a *prima facie* case of obviousness. (Paper No. 20071124 at 2). Respectfully, we submit that the rejection is devoid of *any* evidence - or “reasoning” - in support of the proposed modification of Hoshino. And, the *KSR* opinion referenced by the Examiner does not cure the noted infirmities in the rejection. In fact, the Supreme Court in *KSR* stated that the obviousness “***analysis should be made explicit***” and the teaching-suggestion-motivation test is “***a helpful insight***” for determining obviousness. *KSR*, 127 S.Ct. at 1731-32. See also *Ex parte Noelle*, 2008 WL 55123, \*4 (BPAI Jan. 3, 2008) (citing *KSR*) (“In making an obviousness determination over a combination of prior art references, it is important to ***identify a reason why*** persons of ordinary skill in the art would have attempted to make the claimed subject matter.”) (emphasis added).

Here, what the rejection should have done, but did not, was to explain on the record ***why*** one skilled in this art would modify the disclosure of Hoshino to arrive at the claimed process. As set forth above, Hoshino discloses the conversion of L-

sorbose to **2-KGA** by aldehyde dehydrogenase, but the rejection is silent on where in Hoshino the conversion of L-sorbose to **vitamin C** by the same aldehyde dehydrogenase is disclosed. In contrast, claim 1 of the instant application recites “wherein **the conversion of L-sorbose to vitamin C is catalyzed by the purified L-sorbose dehydrogenase** in the presence of an electron acceptor.” Because, as noted above, the rejection did not carry out a proper analysis, it failed to recognize this factual gap. And, not surprisingly, it also failed to explain how that factual gap in Hoshino is bridged to arrive at the claimed subject matter.

The Examiner’s bald assertion that “[o]ne of ordinary skilled [*sic*] in the art would reasonably expect to prepare L-sorbose utilizing the **ADL** which would be further processed to produce vitamin C based on [Honma]” is a conclusion masquerading as reasoning. Further obscuring the rejection is the Examiner’s discussion of the preparation of L-sorbose or “ADL”. (Paper No. 20071124 at 3). The instant application does not claim the production of L-sorbose or the use of “ADL.” (*Id.*). At bottom, the Examiner’s only alleged support for the unpatentability of claims 1-4 falls short. For this reason also the rejection should be withdrawn.

Further undermining the rejection is the Examiner’s own concession that there is no motivation to modify Hoshino to arrive at the instant disclosure. In a previous Office Action dated August 7, 2007 (well after the Supreme Court’s *KSR* opinion), the Examiner acknowledged that “**the art of record do [*sic*] not suggest or motivate one of ordinary skilled [*sic*] in the art to recover Vitamin C from the fermentation medium based on US 6,242,233 as a direct synthesis without an**

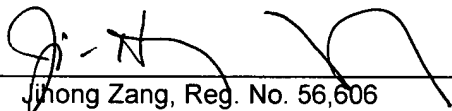
additional step.” (Paper No. 20070801 at 3, emphasis added). Thus, based on the Examiner’s own admissions, which have not been refuted or disavowed, the present rejection cannot stand and must be withdrawn.

Moreover, the presently claimed process provides unexpected and superior results, which would not have been expected by a skilled artisan. As set forth above, the rejection did not identify any disclosure or suggestion in Hoshino regarding the ability of L-sorbose dehydrogenase to convert L-sorbose directly into vitamin C. The presently claimed process is based on the unforeseeable and unexpected dual function of the enzyme, which is capable of producing 2-KGA starting from the substrate, L-sorbose, as well as vitamin C starting from the same substrate. The difference between the two reactions lies in the reaction conditions used, e.g., pH, temperature, and process time. For example, in Example 2 of the instant application, it is shown that after incubation of the isolated enzyme for 1 hour in 100 mM potassium phosphate buffer, the amount of vitamin C produced is at least twice the amount of 2-KGA produced at a pH range of about pH 6.6. to 7.8 (See, e.g., Table 2 at page 8). In a process using 25 mM potassium phosphate buffer and a fixed pH of 7.0 for 1 hour, the amount of vitamin C produced was at least 2.5 times higher than that of 2-KGA at a temperature of 20 to 50°C (See, e.g., Table 3 at page 8). The Examiner has not – and cannot – identify any disclosure or suggestion in Hoshino about the dual functions of the enzyme. The ability of one enzyme to convert the same substrate into two different end-products is not "*prima facie* obvious". Indeed, one skilled in this art knows that such enzymes are exceedingly rare. And, thus, to look for such dual functionality in a

particular enzyme, absent some disclosure or suggestion to do so, would not be obvious. In view of the foregoing, it is respectfully submitted that the rejection should be withdrawn.

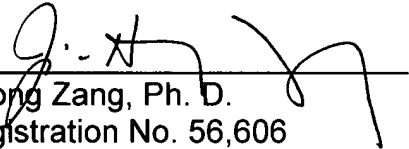
Accordingly, for the reasons set forth above, entry of the amendments, reconsideration, withdrawal of the rejection, and allowance of the claims are respectfully requested. If the Examiner has any questions regarding this paper, please contact the undersigned.

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on June 6, 2008.

  
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